

SEQUENCE LISTING

<110> Borean Pharma A/S

<120> Cleavage of fusion proteins using Granzyme B protease

<130> 3106

<160> 57

<170> PatentIn version 3.2

<210> 1

<211> 243

<212> PRT

<213> Artificial

<220>

<223> pro-IEGR-GrB-H6

<400> 1

Met Gly Ser Ile Glu Gly Arg Ile Ile Gly Gly His Glu Ala Lys Pro
1 5 10 15His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
165 170 175Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
180 185 190Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

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<400> 2

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
 85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225 230 235 240

His His His

<210> 3
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<223> pro-IEAD-GrB-H6

<400> 3

Met Gly Ser Ile Glu Ala Asp Ile Ile Gly Gly His Glu Ala Lys Pro
1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

<210> 4
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 <223> pro-IEPD-GrB-H6 C228S

<400> 4

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
 85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Ser Thr Lys Val Ser Ser Phe Val
210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225 230 235 240

His His His

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<213> Artificial

<220>
<223> pro-IEPD-GrB-H6 C228A

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Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Ala Thr Lys Val Ser Ser Phe Val
210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225 230 235 240

His His His

<210> 6
<211> 243
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<213> Artificial

<220>
<223> pro-IEPD-GrB-H6 C228T

<400> 6

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Thr Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

<210> 7
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 <223> pro-IEPD-GrB-H6 C228V

<400> 7

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
 85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Val Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

<210> 8
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 <212> PRT
 <213> Artificial

<220>
 <223> pro-IEPD-GrB-H6 C228F

<400> 8

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
 85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Phe Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

<210> 9
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 <212> DNA
 <213> Artificial

<220>
 <223> H6 C-term fw

<400> 9
 catggacgga agcttgaatt cacatcacca tcaccatcac taacgc 46

<210> 10
 <211> 46
 <212> DNA
 <213> Artificial

<220>
 <223> H6 C-term rev

<400> 10
 aattgcgta gtgatggatga tggatgatgtg aattcaagct tccgct 46

<210> 11
 <211> 40
 <212> DNA
 <213> Artificial

<220>
 <223> GrBfw primer

<400> 11
 catgggatcc atcgagggtg ggatcatcgg gggacatgag 40

<210> 12
 <211> 38
 <212> DNA
 <213> Artificial

<220>
 <223> GrBrev EcoRI primer

<400> 12
 gcgtgaattc aggtaccgtt tcatggtttt ctttatcc 38

<210> 13
 <211> 715
 <212> DNA
 <213> Artificial

<220>
 <223> GrB EcoRI fragment

<400> 13
 catgggatcc atcgagggtg ggatcatcgg gggacatgag gccaagcccc actcccgccc 60
 ctacatggct tatcttatga tctgggatca gaagtctctg aagaggtgcg gtggcttcct 120
 gatacaagac gacttcgtgc tgacagctgc tcaactgttg ggaagctcca taaatgtcac 180
 cttggggggcc cacaatatca aagaacagga gccgaccag cagtttatcc ctgtgaaaag 240
 acccatcccc catccagcct ataatcctaa gaacttctcc aacgacatca tgctactgca 300
 gctggagaga aaggccaagc ggaccagagc tgtgcagccc ctcaggctac ctagcaacaa 360
 ggcccaggtg aagccagggc agacatgcag tgtggccggc tgggggcaga cggccccct 420
 gggaaaacac tcacacacac tacaagaggt gaagatgaca gtgcaggaag atcgaaagtg 480
 cgaatctgac ttacgccatt attacgacag taccattgag ttgtgctgg gggaccaga 540
 gattaaaaag acttccttta agggggactc tggaggccct cttgtgtgta acaaggtggc 600
 ccagggcatt gtctcctatg gacgaaacaa tggcatgcct ccacgagcct gcaccaaagt 660
 ctcaagcttt gtacactgga taaagaaaac catgaaacgg tacctgaatt cacgc 715

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 <211> 33
 <212> DNA
 <213> Artificial

<220>
 <223> GrB GR-PD fw

<400> 14
 tccatcgagc cggatatcat cgggggacat gag 33

<210> 15
 <211> 34
 <212> DNA
 <213> Artificial

<220>
 <223> GrB GR-PD rev

<400> 15
 ccccgatgat atccggctcg atggatccca tatg 34

<210> 16
 <211> 33
 <212> DNA
 <213> Artificial

<220>
 <223> GrB GR-AD fw

<400> 16
 tccatcgagg ctgatatcat cgggggacat gag 33

<210> 17
<211> 34
<212> DNA
<213> Artificial

<220>
<223> GrB GR-AD rev

<400> 17
ccccgatgat atcagcctcg atggatccca tatg 34

<210> 18
<211> 27
<212> DNA
<213> Artificial

<220>
<223> GrB SAT fw

<400> 18
tccacgagca dccaccaaag tctcaag 27

<210> 19
<211> 26
<212> DNA
<213> Artificial

<220>
<223> GrB SAT rev

<400> 19
agactttggt gghggctcgt ggaggc 26

<210> 20
<211> 27
<212> DNA
<213> Artificial

<220>
<223> GrB VF fw

<400> 20
tccacgagcc ktcaccaaag tctcaag 27

<210> 21
<211> 26
<212> DNA
<213> Artificial

<220>
<223> GrB VF rev

<400> 21
agactttggt gamggctcgt ggaggc 26

<210> 22
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<212> PRT
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<220>
<223> H6-TripUB IEPD!SP

<400> 22

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Glu Pro Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 23
<211> 338
<212> PRT
<213> Artificial

<220>
<223> H6-IEPD-RAP

<400> 23

Met Gly Ser His His His His His His Gly Ser Ile Glu Pro Asp Tyr
1 5 10 15

Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro Lys Arg Glu Ser Gly
20 25 30

Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu Trp Glu Lys Ala Gln
35 40 45

Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu Leu His Ala Asp Leu
50 55 60

Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys Lys Leu Lys Leu Asp
65 70 75 80

Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg Leu Ile Arg Asn Leu
85 90 95

Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly Lys Lys Asp Ala Arg
100 105 110

Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln Glu Asp Gly Leu Asp
115 120 125

Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr Ser Gly Lys
130 135 140

Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg Glu Phe Leu His His
145 150 155 160

Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu Glu Thr Leu Ser Arg
165 170 175

Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro Ser Asp Leu Ser Asp
180 185 190

Ile Lys Gly Ser Val Leu His Ser Arg His Thr Glu Leu Lys Glu Lys
195 200 205

Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Arg Val Ser His
210 215 220

Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu Pro Arg Val Ile Asp
225 230 235 240

Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr Asp Lys Glu Leu Glu
245 250 255

Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile Glu Lys His
260 265 270

Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His Glu Lys Leu Arg His
275 280 285

Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser Arg Glu Lys
290 295 300

His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr Thr Val Lys
305 310 315 320

Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala Arg His Asn
325 330 335

Glu Leu

<210> 24
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<212> PRT
<213> Artificial

<220>

<223> H6Ubi-IEPD-ApoA1

<400> 24

Met Gly Ser His His His His His His Gly Ser Gln Ile Phe Val Lys
1 5 10 15

Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr
20 25 30

Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro
35 40 45

Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg
50 55 60

Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val
65 70 75 80

Leu Arg Leu Arg Gly Gly Ser Ile Glu Pro Asp Gly Gly Asp Glu Pro
85 90 95

Pro Gln Ser Pro Trp Asp Arg Val Lys Asp Leu Ala Thr Val Tyr Val
100 105 110

Asp Val Leu Lys Asp Ser Gly Arg Asp Tyr Val Ser Gln Phe Glu Gly
115 120 125

Ser Ala Leu Gly Lys Gln Leu Asn Leu Lys Leu Leu Asp Asn Trp Asp
130 135 140

Ser Val Thr Ser Thr Phe Ser Lys Leu Arg Glu Gln Leu Gly Pro Val
145 150 155 160

Thr Gln Glu Phe Trp Asp Asn Leu Glu Lys Glu Thr Glu Gly Leu Arg
165 170 175

Gln Glu Met Ser Lys Asp Leu Glu Glu Val Lys Ala Lys Val Gln Pro
180 185 190

Tyr Leu Asp Asp Phe Gln Lys Lys Trp Gln Glu Glu Met Glu Leu Tyr
195 200 205

Arg Gln Lys Val Glu Pro Leu Arg Ala Glu Leu Gln Glu Gly Ala Arg
210 215 220

Gln Lys Leu His Glu Leu Gln Glu Lys Leu Ser Pro Leu Gly Glu Glu
225 230 235 240

Met Arg Asp Arg Ala Arg Ala His Val Asp Ala Leu Arg Thr His Leu
245 250 255

Ala Pro Tyr Ser Asp Glu Leu Arg Gln Arg Leu Ala Ala Arg Leu Glu
260 265 270

Ala Leu Lys Glu Asn Gly Gly Ala Arg Leu Ala Glu Tyr His Ala Lys
275 280 285

Ala Thr Glu His Leu Ser Thr Leu Ser Glu Lys Ala Lys Pro Ala Leu
290 295 300

Glu Asp Leu Arg Gln Gly Leu Leu Pro Val Leu Glu Ser Phe Lys Val
305 310 315 320

Ser Phe Leu Ser Ala Leu Glu Glu Tyr Thr Lys Lys Leu Asn Thr Gln
325 330 335

<210> 25
<211> 197
<212> PRT
<213> Artificial

<220>
<223> H6-IEPD-TN123

<400> 25

Met Gly Ser His His His His His His Gly Ser Ile Glu Pro Asp Gly
1 5 10 15

Glu Pro Pro Thr Gln Lys Pro Lys Lys Ile Val Asn Ala Lys Lys Asp
20 25 30

Val Val Asn Thr Lys Met Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr
35 40 45

Leu Ala Gln Glu Val Ala Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr
50 55 60

Val Cys Leu Lys Gly Thr Lys Val His Met Lys Cys Phe Leu Ala Phe
65 70 75 80

Thr Gln Thr Lys Thr Phe His Glu Ala Ser Glu Asp Cys Ile Ser Arg
85 90 95

Gly Gly Thr Leu Ser Thr Pro Gln Thr Gly Ser Glu Asn Asp Ala Leu
100 105 110

Tyr Glu Tyr Leu Arg Gln Ser Val Gly Asn Glu Ala Glu Ile Trp Leu
115 120 125

Gly Leu Asn Asp Met Ala Ala Glu Gly Thr Trp Val Asp Met Thr Gly
130 135 140

Ala Arg Ile Ala Tyr Lys Asn Trp Glu Thr Glu Ile Thr Ala Gln Pro
145 150 155 160

Asp Gly Gly Lys Thr Glu Asn Cys Ala Val Leu Ser Gly Ala Ala Asn
165 170 175

Gly Lys Trp Phe Asp Lys Arg Cys Arg Asp Gln Leu Pro Tyr Ile Cys
180 185 190

Gln Phe Gly Ile Val
195

<210> 26
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IQAD!SP
<400> 26

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Gln Ala Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 27
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IQAD!SG
<400> 27

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Gln Ala Asp Ser Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 28
<211> 150
<212> PRT
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<220>
<223> H6-TripUB VGPD!SP

<400> 28

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Val
1 5 10 15

Gly Pro Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
 115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
 130 135 140

Arg Leu Arg Gly Gly Ser
 145 150

<210> 29
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 <212> PRT
 <213> Artificial

<220>
 <223> H6-TripUB VGPD!FG

<400> 29

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Val
 1 5 10 15

Gly Pro Asp Phe Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
 20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
 35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
 50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
 65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
 85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
 100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
 115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
 130 135 140

Arg Leu Arg Gly Gly Ser
 145 150

<210> 30
 <211> 143
 <212> PRT
 <213> Artificial

<220>
 <223> H6-TripUB IEPD!TQ

<400> 30

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
 1 5 10 15

Glu Pro Asp Thr Gln Lys Pro Lys Lys Ile Val Asn Ala Lys Lys Asp
 20 25 30

Val Val Asn Thr Lys Met Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr
 35 40 45

Leu Ala Gln Glu Val Ala Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr
 50 55 60

Val Gly Ser Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr
 65 70 75 80

Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile
 85 90 95

Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala
 100 105 110

Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln
 115 120 125

Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Ser
 130 135 140

<210> 31
 <211> 137
 <212> PRT
 <213> Artificial

<220>
 <223> H6-TripUB IEPD!IV

<400> 31

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
 1 5 10 15

Glu Pro Asp Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met
 20 25 30

Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala
 35 40 45

Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe
 50 55 60

Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser
 65 70 75 80

Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile
 85 90 95

Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp
 100 105 110

Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His
 115 120 125

Leu Val Leu Arg Leu Arg Gly Gly Ser
 130 135

<210> 32
 <211> 150
 <212> PRT
 <213> Artificial

<220>
 <223> H6-TripUB IEPD!EP

<400> 32

Met Gly Ser His His His His His Gly Ser Gly Ser Gly Ser Ile
 1 5 10 15

Glu Pro Asp Glu Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
 20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
 35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
 50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
 65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
 85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
 100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
 115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
 130 135 140

Arg Leu Arg Gly Gly Ser
 145 150

<210> 33
 <211> 150
 <212> PRT
 <213> Artificial

<220>
 <223> H6-TripUB IEPD!EG

<400> 33

Met Gly Ser His His His His His Gly Ser Gly Ser Gly Ser Ile
 1 5 10 15

Glu Pro Asp Glu Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 34
<211> 37
<212> DNA
<213> Artificial

<220>
<223> TripUB GrB fw primer

<400> 34
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37

<210> 35
<211> 38
<212> DNA
<213> Artificial

<220>
<223> TripUB GrB rev primer

<400> 35
ggtaccagga gagtcaggct cgatggatcc actaccac

38

<210> 36
<211> 34
<212> DNA
<213> Artificial

<220>
<223> RAP GrB fw primer

<400> 36
cgatccatc gagcctgact actcgcgga gaag

34

<210> 37
 <211> 34
 <212> DNA
 <213> Artificial

 <220>
 <223> RAP GrB rev primer

 <400> 37
 cccgcgagta gtcaggctcg atggatccgt gatg 34

 <210> 38
 <211> 42
 <212> DNA
 <213> Artificial

 <220>
 <223> Mut-GrB fw

 <400> 38
 cgtggtgat ccatcgagcc ggacggtgga gatgaacccc cc 42

 <210> 39
 <211> 42
 <212> DNA
 <213> Artificial

 <220>
 <223> Mut-GrB rw

 <400> 39
 ggggggttca tctccaccgt ccggctcgat ggatccacca cg 42

 <210> 40
 <211> 33
 <212> DNA
 <213> Artificial

 <220>
 <223> TN GrB fw primer

 <400> 40
 ggatccatcg agcctgacgg cgagccacca acc 33

 <210> 41
 <211> 33
 <212> DNA
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 <220>
 <223> TN GrB rev primer

 <400> 41
 ggctcgccgt caggctcgat ggatccgtga tgg 33

 <210> 42
 <211> 33
 <212> DNA
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 <220>
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 <400> 42
 ggatccatcc aggcagactc tcctggtacc gag 33

<210> 43
 <211> 34
 <212> DNA
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 <220>
 <223> PC7TripUB GR-AD rev
 <400> 43
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<210> 44
 <211> 37
 <212> DNA
 <213> Artificial
 <220>
 <223> PC7TripUB P-G fw
 <400> 44
 ggatccatcc aggagactc tgggtgtacc gagccac 37

<210> 45
 <211> 38
 <212> DNA
 <213> Artificial
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 <223> PC7TripUB P-G rev
 <400> 45
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<210> 46
 <211> 34
 <212> DNA
 <213> Artificial
 <220>
 <223> DNATrip IE-VG fw
 <400> 46
 gtagtggatc agtcgggcct gactctcctg gtac 34

<210> 47
 <211> 34
 <212> DNA
 <213> Artificial
 <220>
 <223> DNATrip IE-VG rev
 <400> 47
 gagagtcagg cccgactgat ccactaccac tacc 34

<210> 48
 <211> 31
 <212> DNA
 <213> Artificial
 <220>
 <223> DNATrip SP-FG fw
 <400> 48
 ggcctgactt tgggtgtacc gagccaccaa' c 31

<210> 49
<211> 31
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<220>
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<400> 49
ggctcgggtac caccaaagtc aggcccgact g 31

<210> 50
<211> 52
<212> DNA
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<220>
<223> Trip IEPD-TQ

<400> 50
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<210> 51
<211> 54
<212> DNA
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<220>
<223> Trip IEPD-IV

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gggaaaggat ccatcgagcc tgacattgta aatgcccaaga aagatgttgt gaac 54

<210> 52
<211> 39
<212> DNA
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<220>
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<400> 52
cgcaagcttg catgcttagg atccaccag aagtctcaa 39

<210> 53
<211> 29
<212> DNA
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<220>
<223> TripUB EP fw

<400> 53
cgagcctgac gagcctggta ccgagccac 29

<210> 54
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<212> DNA
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<220>
<223> TripUB EP rev

<400> 54
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<210> 55
 <211> 29
 <212> DNA
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<220>
 <223> TripUB EG fw

<400> 55
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<210> 56
 <211> 29
 <212> DNA
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<220>
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<400> 56
 gctcggtagc accctcgta ggctcgatg 29

<210> 57
 <211> 227
 <212> PRT
 <213> Artificial

<220>
 <223> GrB variant C228F

<400> 57

Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg Pro Tyr Met Ala
 1 5 10 15

Tyr Leu Met Ile Trp Asp Gln Lys Ser Leu Lys Arg Cys Gly Gly Phe
 20 25 30

Leu Ile Gln Asp Asp Phe Val Leu Thr Ala Ala His Cys Trp Gly Ser
 35 40 45

Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys Glu Gln Glu Pro
 50 55 60

Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro His Pro Ala Tyr
 65 70 75 80

Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu Gln Leu Glu Arg
 85 90 95

Lys Ala Lys Arg Thr Arg Ala Val Gln Pro Leu Arg Leu Pro Ser Asn
 100 105 110

Lys Ala Gln Val Lys Pro Gly Gln Thr Cys Ser Val Ala Gly Trp Gly
 115 120 125

Gln Thr Ala Pro Leu Gly Lys His Ser His Thr Leu Gln Glu Val Lys
 130 135 140

Met Thr Val Gln Glu Asp Arg Lys Cys Glu Ser Asp Leu Arg His Tyr
145 150 155 160

Tyr Asp Ser Thr Ile Glu Leu Cys Val Gly Asp Pro Glu Ile Lys Lys
165 170 175

Thr Ser Phe Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Asn Lys Val
180 185 190

Ala Gln Gly Ile Val Ser Tyr Gly Arg Asn Asn Gly Met Pro Pro Arg
195 200 205

Ala Phe Thr Lys Val Ser Ser Phe Val His Trp Ile Lys Lys Thr Met
210 215 220

Lys Arg Tyr
225